

6. The array of claim 5, wherein the discrete areas of the solid support contain murine sera.

Q2
7. The array of claim 1, wherein the at least 10 different antibodies is between 100 different antibodies and 10,000 different antibodies.

8. The array of claim 1 further comprising a sample containing a protein derived from human cells.

Sub B2
Q3
15. A device comprising an array of 10 reaction sites in a pre-selected pattern, wherein each reaction site contains an antibody that specifically binds a protein wherein the antibody is correlated on a one-to-one basis with an isolated polynucleotide sequence encoding the protein to which the antibody specifically binds.

16. The device of claim 15 wherein each reaction site is comprised of murine antibodies.

19. The device of claim 15 wherein at least 10% of the reaction sites of the array is comprised of aliquots of homogenous antibodies.

Q4
20. The device of claim 15 wherein at least one reaction site contains murine sera.

Please cancel claims 9-14 and 21 without prejudice.

Applicant affirms the election as recited in the last Action.

Claim Rejections – 35 USC § 112

The claim rejections detailed at paragraph 3 of the action are remedied in the amended claims. Specifically, claim 1 is amended for definiteness purposes to specify that the antigen is the entity to which the antibodies in the array specifically bind, that the antibodies at each point of the array bind to different antigens, and thus that the antibodies are binding to the antigens, not to any polynucleotide sequence. The term “correlated to” means that the antibody may be correlated to the polynucleotide sequence because the polynucleotide sequence is used to generate the antigen to which the antibody specifically binds. The correlation aspect refers to a preferred embodiment of the invention in which the antibody may be raised through DNA immunization using the polynucleotide sequence, as described in the specification, and thus, the polynucleotide sequence is known and correlated to the antibody. It is believed that this language is sufficiently definite when read in light of the specification.

In claim 6, the language is revised to simply indicate that the array may contain murine sera, again as when the antibodies are derived from a preferred embodiment of the invention. The language “a component of” is deleted as redundant.

In claim 7, the recitation of numerical values is amended to specify that the array contains between 100 different antibodies and 10,000 different antibodies.

In claim 8, the language is recited to simply specify that the sample contains a protein derived from human cells.

Claim 15 is amended to specify that the antibody binds a protein and is correlated to an isolated polynucleotide sequence encoding the protein. The antecedent basis issue is rectified and the claim is clarified in the manner of claim 1 above to add definiteness to the claim language.

The typographical error in claim 16 is rectified.

The typographical error in claim 19 is rectified and the language of claim 20 is amended in the manner of claim 6 above.

35 USC § 103 – The Pending Claims Cannot Be Rendered Obvious Under Section 103 of Title 35
Because a *Prima Facie* Case Cannot Exist Based on a Combination of the Cited References.

None of claims 1-8 or 15-20 are rendered obvious over Wagner et al. in view of Kamb.

Applicants respectfully submit that the Examiner has not satisfied the initial burden of factually supporting a *prima facie* conclusion of obviousness. See M.P.E.P. §2142. The Examiner has not met the initial burden to show that the invention as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. The question of obviousness is not merely whether a combination of the prior art was possible, but rather whether the specific combination would have been made to yield each and every element of the invention in the manner claimed by Applicants here. Thus, the combination must be proper and the combination must actually yield the claimed invention, if not, a *prima facie* case does not exist. See 35 U.S.C. 103; *In re Dembiczak*, 50 USPQ2d 1614, 17-18 (Fed. Cir. 1999); *In re Kotzab*, 55 USPQ2d 1314, 1317 (Fed. Cir. 2000); MPEP § 2142. A rejection pursuant to §103(a) requires a particular finding that justifies a conclusion that the skilled artisan would have had the motivation to combine the prior art

to reach the invention claimed. On this point, the MPEP states: "the mere fact that the references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." M.P.E.P. §2143.01.

More particularly, Federal Circuit precedent requires that: "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed." *In re Kotzab*, 55 USPQ2d 1314, 1317 (Fed. Cir. 2000) (emphasis added). In the present case, no such finding can be made based on the implied or inherent teachings of Wagner et al. or Kamb without resort to the present invention or the suggestion to select the individual elements of the array as claimed and to specifically correlate the antibodies to the polynucleotide sequences as in the present claims. Accordingly, Applicants respectfully request that the pending claims be reconsidered and allowed.

Referring specifically to paragraph 15 of the office action and the merits of the § 103 issue, Applicant submits that the Wagner et al. and Kamb references cannot be combined to establish a *prima facie* case against the claims of the present invention because even the combination does not contain each element of the pending claims. Two well established principles of the law of obviousness under 35 U.S.C. § 103 are "(B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination" and "(C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention," See MPEP § 2141, Basic Considerations Which Apply to Obviousness Rejections.

A combination containing Kamb should not be used in any obviousness rejection of these claims because Kamb addresses antibodies that bind polynucleotide sequences and not antibodies

that bind antigens that are encoded by the polynucleotide sequences and which antibodies are correlated to the sequence as recited in the pending claims. The only rationale identified by the Examiner for the combination on which the § 103 rejection is based relates to a motivation derived from the teachings of Kamb to use polynucleotide-specific antibodies. Thus, the very rationale for the § 103 *prima facie* case is inapposite to the present claims. The Examiner has not identified any specific motivation in either of the cited prior art references, or elsewhere, for one of ordinary skill to combine the references to reach the substance of the claimed invention. As recently stated by the Court of Appeals for the Federal Circuit in In re Dembiczak:

Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. See, e.g., *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998) (describing "teaching or suggestion or motivation [to combine]" as an "essential evidentiary component of an obviousness holding"); *In re Rouffet*, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) ("the Board must identify specifically . . . the reasons one of ordinary skill in the art would have been motivated to select the references and combine them"); *In re Fritch*, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (examiner can satisfy burden of obviousness in light of combination "only by showing some objective teaching [leading to the combination]"); *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) (evidence of teaching or suggestion "essential" to avoid hindsight); *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 297, 227 USPQ 657, 667 (Fed. Cir. 1985) (district court's conclusion of obviousness was error when it "did not elucidate any factual teachings, suggestions or incentives from this prior art that showed the propriety of combination"). See also *Graham*, 383 U.S. at 18, 148 USPQ at 467 ("strict observance" of factual predicates to obviousness conclusion required). Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability--the essence of hindsight. See, e.g., *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1138, 227 USPQ 543, 547 (Fed. Cir. 1985) ("The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time."). In this case, the Board fell into the hindsight trap.

We have noted that evidence of a suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved, see *Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1630 (Fed. Cir. 1996), *Para-Ordinance Mfg. v. SGS Imports*

Intern., Inc., 73 F.3d 1085, 1088, 37 USPQ2d 1237, 1240 (Fed. Cir. 1995), although "the suggestion more often comes from the teachings of the pertinent references," Rouffet, 149 F.3d at 1355, 47 USPQ2d at 1456. The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular. See, e.g., C.R. Bard, 157 F.3d at 1352, 48 USPQ2d at 1232. Broad conclusory statements regarding the teaching of multiple references, standing alone, are not "evidence." . . . [50 USPQ2d 1614, 1617-1618 (Fed. Cir. 1999)].

Furthermore, absent an identified rationale to create the array with antibodies correlated to polynucleotides as claimed, the only source for the teachings to create the claimed invention is Applicant's own teaching. As stated by the Federal Circuit in *In re Kotzab*,

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. See *Dembiczak*, 175 F.3d at 999, 50 USPQ2d at 1617. Close adherence to this methodology is especially important in case where the very ease with which the invention can be understood may prompt one to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher. *Id.* (quoting *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 313 (Fed. Cir. 1983).

Therefore, without referring to the present invention, no reason exists for the skilled artisan to modify the teachings of Wagner et al. or Kamb to yield the composition of the claims. The motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention. See, *In re Napier*, 55 F.3d 610, 613, 34 U.S.P.Q.2d 1782, 1784 (Fed. Cir. 1995) ("Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination."). In the present case, no rationale is offered in the context of the present claims and without a specific finding of rationale to

modify the prior art reference, the obviousness rejection cannot be maintained, see *In re Kotzab*,
supra.

In light of the above, applicant requests favorable consideration and allowance of the pending claims. If the Examiner has any questions regarding the foregoing, or if the Examiner believes that an interview would facilitate the examination of this application, or if any additional information is required, the Examiner is invited to contact the undersigned at 949/567-6700, X 6740.

Respectfully submitted,

ORRICK, HERRINGTON &
SUTCLIFFE LLP

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By: 

Kurt T. Mulville
Reg. No. 37,194

1900 Main Street
Sixth Floor
Irvine, CA 92614
949/567-6700 X 6740 Telephone
949/567-6710 Facsimile